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<110> Memorial Sloan-Kettering Cancer Center
Kolesnick, Richard N.
Xing, Hong-Mei R.

<120> KINASE SUPPRESSOR OF RAS INACTIVATION FOR THERAPY OF RAS MEDIATED
TUMORIGENESIS

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<140> US 10/727,358

<141> 2003-12-03

<150> 60/384,228

<151> 2002-05-30

<150> 60/460,023

<151> 2003-04-03

<150> PCT/US03/16961

<151> 2003-05-29

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<170> PatentIn version 3.1

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Ser Ile Gly Ser Leu Arg Gly Leu Arg Thr Lys Cys Ser Val Ser Asn
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Tyr Ile Cys Lys Gln Gln Gln Ser Lys Leu Ser Val Thr Pro Ser Asp
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Arg Thr Ala Glu Leu Asn Ser Tyr Pro Arg Phe Ser Asp Trp Leu Tyr
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Ile Phe Asn Val Arg Pro Glu Val Val Gln Glu Ile Pro Gln Glu Leu
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Thr Leu Asp Ala Leu Leu Glu Met Asp Glu Ala Lys Ala Lys Glu Met
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Pro Pro Met Asp Met Leu Ser Ser Leu Gly Arg Ala Gly Ala Ser Thr
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Pro Gln Leu Val Arg Arg Asp Ile Gly Leu Ser Val Thr His Arg Phe
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Met Ile Phe Gly Val Lys Cys Lys His Cys Arg Leu Lys Cys His Asn
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Pro Glu Ala Gly Lys Ser Glu Ala Glu Asp Asp Glu Glu Asp Glu Val
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Lys Ala Ser Gln Thr Ser Val Tyr Leu Gln Glu Trp Asp Ile Pro Phe
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Gly Arg Thr Leu His Ser Phe Val Arg Asp Pro Lys Thr Ser Leu Asp
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Leu Ser His Asp Trp Leu Cys Tyr Leu Ala Pro Glu Ile Val Arg Glu
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Met Ile Pro Gly Arg Asp Glu Asp Gln Leu Pro Phe Ser Lys Ala Ala
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Trp Pro Phe Lys His Gln Pro Ala Glu Ala Leu Ile Trp Gln Ile Gly
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Arg Pro Ser Phe Ser Leu Leu Met Asp Met Leu Glu Arg Leu Pro Lys
820 825 830

Leu Asn Arg Arg Leu Ser His Pro Gly His Phe Trp Lys Ser Ala Asp
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Leu Gln Lys Leu Ile Asp Ile Ser Ile Gly Ser Leu Arg Gly Leu Arg
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Thr Lys Cys Ala Val Ser Asn Asp Leu Thr Gln Gln Glu Ile Arg Thr
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Leu Glu Ala Lys Leu Val Arg Tyr Ile Cys Lys Gln Arg Gln Cys Lys
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Leu Ser Val Ala Pro Gly Glu Arg Thr Pro Glu Leu Asn Ser Tyr Pro
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Arg Phe Ser Asp Trp Leu Tyr Thr Phe Asn Val Arg Pro Glu Val Val
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Gln Glu Ile Pro Arg Asp Leu Thr Leu Asp Ala Leu Leu Glu Met Asn
115 120 125

Glu Ala Lys Val Lys Glu Thr Leu Arg Arg Cys Gly Ala Ser Gly Asp
130 135 140

Glu Cys Gly Arg Leu Gln Tyr Ala Leu Thr Cys Leu Arg Lys Val Thr
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Gly Leu Gly Gly Glu His Lys Glu Asp Ser Ser Trp Ser Ser Leu Asp
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| Ser Asp Ser Pro Thr Pro Ser Phe Ser Glu Gly Leu Ser Asp Thr Cys | | |
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| Ile Pro Leu His Ala Ser Gly Arg Leu Thr Pro Arg Ala Leu His Ser | | |
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| Phe Ile Thr Pro Pro Thr Thr Pro Gln Leu Arg Arg His Thr Lys Leu | | |
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| Leu Pro Ser Phe Pro Thr Leu Thr Arg Arg Lys Ser His Glu Ser Gln | | |
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| His Arg Phe Ser Thr Lys Ser Trp Leu Ser Gln Val Cys His Val Cys | | |
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| Asn Asn Pro Val Asp Arg Ala Ala Glu Pro His Phe Gly Thr Leu Pro | | |
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Ala Pro Phe Pro Thr Ser Ser Asn Pro Ser Ser Ala Thr Thr Pro Pro
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Asn Pro Ser Pro Gly Gln Arg Asp Ser Arg Phe Asn Phe Pro Ala Ala
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Tyr Phe Ile His His Arg Gln Gln Phe Ile Phe Pro Asp Ile Ser Ala
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Phe Ala His Ala Ala Pro Leu Pro Glu Ala Ala Asp Gly Thr Arg Leu
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Phe Glu Gln Val Glu Leu Gly Glu Pro Ile Gly Gln Gly Arg Trp Gly
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Arg Val His Arg Gly Arg Trp His Gly Glu Val Ala Ile Arg Leu Leu
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Glu Met Asp Gly His Asn Gln Asp His Leu Lys Leu Phe Lys Lys Glu
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Val Met Asn Tyr Arg Gln Thr Arg His Glu Asn Val Val Leu Phe Met
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Lys Gly Arg Thr Leu His Ser Phe Val Arg Asp Pro Lys Thr Ser Leu
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Gly Tyr Leu His Ala Lys Gly Ile Val His Lys Asp Leu Lys Ser Lys
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Asn Val Phe Tyr Asp Asn Gly Lys Val Val Ile Thr Asp Phe Gly Leu
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Phe Gly Ile Ser Gly Val Val Arg Glu Gly Arg Arg Glu Asn Gln Leu
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Glu Met Thr Pro Gly Lys Asp Glu Asp Gln Leu Pro Phe Ser Lys Ala
755 760 765

Ala Asp Val Tyr Ala Phe Gly Thr Val Trp Tyr Glu Leu Gln Ala Arg
770 775 780

Asp Trp Pro Leu Lys Asn Gln Ala Ala Glu Ala Ser Ile Trp Gln Ile
785 790 795 800

Gly Ser Gly Glu Gly Met Lys Arg Val Leu Thr Ser Val Ser Leu Gly
805 810 815

Lys Glu Val Ser Glu Ile Leu Ser Ala Cys Trp Ala Phe Asp Leu Gln
820 825 830

Glu Arg Pro Ser Phe Ser Leu Leu Met Asp Met Leu Glu Lys Leu Pro
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| ccgaagccca cccatgggct ggctctggga ggcaatggcg ctgagtatgg gggcatctct | 1920 |
| cgcattggatc cccacagatg gtacggaggg atatcgggct gtcggtgacg cacaggttct | 1980 |
| ccaccaagtc ctggctgtcg caggctctgcc acgtgtgcca gaagagcatg atatttggag | 2040 |
| tgaagtgcaa gcattgcagg ttgaagtgtc acaacaaatg taccaaagaa gccctgcct | 2100 |
| gtagaatatc cttcctgcca ctaactcggc ttcggaggac agaactctgt ccctcggaca | 2160 |
| tcaacaaccc ggtggacaga gcagccgaac cccatttttg aaccctcccc aaagcactga | 2220 |

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| caaagaagga | gcaccctccg | gccatgaatc | acctggactc | cagcagcaac | ccttcctcca | 2280 |
| ccacctcctc | cacaccctcc | tcaccggcgc | ccttcccgac | atcatccaac | ccatccagcg | 2340 |
| ccaccacgcc | ccccaaaccc | tcacctggcc | agcgggacag | caggttcaac | ttcccagctg | 2400 |
| cctacttcat | tcatcataga | cagcagttta | tctttccaga | catttcagcc | tttgcacacg | 2460 |
| cagccccgct | ccctgaagct | gccgacggta | cccggctcga | tgaccagccg | aaagcagatg | 2520 |
| tgttggaagc | tcacgaagcg | gaggctgagg | agccagaggc | tggcaagtca | gaggcagaag | 2580 |
| acgatgagga | cgagggtggac | gacttgccga | gctctcgccg | gccctggcgg | ggccccatct | 2640 |
| ctcgcaaggc | cagccagacc | agcgtgtacc | tgcaggagtg | ggacatcccc | ttcgagcagg | 2700 |
| tagagctggg | cgagcccatc | gggcagggcc | gctggggccg | ggtgcaccgc | ggccgctggc | 2760 |
| atggcgaggt | ggccattcgc | ctgctggaga | tggacggcca | caaccaggac | cacctgaagc | 2820 |
| tcttcaagaa | agagggtgatg | aactaccggc | agacgcggca | tgagaacgtg | gtgctcttca | 2880 |
| tgggggcctg | catgaaccgc | ccccacctgg | ccattatcac | cagcttctgc | aaggggcgga | 2940 |
| cgttgcactc | gtttgtgagg | gacccaaga | cgtctctgga | catcaacaag | acgaggcaaa | 3000 |
| tcgctcagga | gatcatcaag | ggcatgggat | atcttcatgc | caagggcatc | gtacacaaaag | 3060 |
| atctcaaadc | taagaacgtc | ttctatgaca | acggcaaggc | ggtcatcaca | gacttcgggc | 3120 |
| tgtttgggat | ctcaggcgctg | gtccgagagg | gacggcgctga | gaaccagcta | aagctgtccc | 3180 |
| acgactggct | gtgctatctg | gcccttgaga | ttgtacgcga | gatgaccccc | gggaaggacg | 3240 |
| aggatcagct | gccattctcc | aaagctgctg | atgtctatgc | atttgggact | gtttgggatg | 3300 |
| agctgcaagc | aagagactgg | cccttgaaga | accaggctgc | agaggcatcc | atctggcaga | 3360 |
| ttggaagcgg | ggaaggaatg | aagcgtgtcc | tgacttctgt | cagcttgggg | aaggaagtca | 3420 |
| gtgagatcct | gtcggcctgc | tgggctttcg | acctgcagga | gagaccagc | ttcagcctgc | 3480 |
| tgatggacat | gctggagaaa | cttcccaagc | tgaaccggcg | gctctccac | cctggacact | 3540 |
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| cctaataaac | aactcagcac | cgtgacttct | gctaaaatgc | aaaatgagat | gcgggcacta | 3660 |
| accaggggga | tgccacctct | gctgctccag | tcgtctctct | cgaggctact | tcttttgctt | 3720 |
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24

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<223> primer

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<220>

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| aagaaggagc | accctccggc | catgaatcac | ctggactcca | gcagcaaccc | ttcctccacc | 1320 |
| acctectcca | caccctctc | accggcgccc | ttcccgacat | catccaaccc | atccagcgcc | 1380 |
| accacgcccc | ccaaccctc | acctggccag | cgggacagca | ggttcaactt | cccagctgcc | 1440 |
| tacttcattc | atcatagaca | gcagtttatc | tttcagaca | tttcagcctt | tgcacacgca | 1500 |
| gccccgctcc | ctgaagctgc | cgacgggtacc | cggctcgatg | accagccgaa | agcagatgtg | 1560 |
| ttggaagctc | acgaagcggg | ggctgaggag | ccagaggctg | gcaagtcaga | ggcagaagac | 1620 |
| gatgaggacg | aggtggacga | cttgccgagc | tctcgccggc | cctggcgggg | ccccatctct | 1680 |
| cgcaaggcca | gccagaccag | cgtgtacctg | caggagtggg | acatcccctt | cgagcaggta | 1740 |
| gagctgggcg | agcccatcgg | gcagggccgc | tggggccggg | tgcaccgcgg | ccgctggcat | 1800 |
| ggcgagggtg | ccattcgcct | gctggagatg | gacggccaca | accaggacca | cctgaagctc | 1860 |
| ttcaagaaag | aggtgatgaa | ctaccggcag | acgcggcgatg | agaacgtggg | gctcttcatg | 1920 |
| ggggcctgca | tgaaccgcgc | ccacctggcc | attatcacca | gcttctgcaa | ggggcggacg | 1980 |
| ttgcactcgt | ttgtgaggga | ccccagacg | tctctggaca | tcaacaagac | gaggcaaatc | 2040 |
| gctcaggaga | tcataaagg | catgggatat | cttcattgcca | agggcatcgt | acacaaagat | 2100 |
| ctcaaatacta | agaacgtctt | ctatgacaac | ggcaagggtg | tcatacacaga | cttcgggctg | 2160 |
| tttgggatct | caggcgtggg | ccgagaggga | cggcgtgaga | accagctaaa | gctgtcccac | 2220 |
| gactggctgt | gctatctggc | ccctgagatt | gtacgcgaga | tgacccccgg | gaaggacgag | 2280 |
| gatcagctgc | cattctccaa | agctgctgat | gtctatgcat | ttgggactgt | ttggtatgag | 2340 |
| ctgcaagcaa | gagactggcc | cttgaagaac | caggctgcag | aggcatccat | ctggcagatt | 2400 |
| ggaagcgggg | aaggaatgaa | gcgtgtcctg | acttctgtca | gcttggggaa | ggaagtcagt | 2460 |
| gagatcctgt | cggcctgctg | ggctttcgac | ctgcaggaga | gaccagctt | cagcctgctg | 2520 |
| atggacatgc | tggagaaact | tccaagctg | aaccggcggc | tctcccaccc | tggacacttc | 2580 |
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Leu Glu Ala Lys Leu Val Arg Tyr
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